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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,484	CHOO ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,8,10,11,13-15,21-26,31,34,35 and 38* is/are pending in the application.

4a) Of the above claim(s) *1,2,4,5,7,8,10,11,13-15,21-26,31,35 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 12 August 2005 in response to the Non-Final Office Action mailed 16 May 2005. Claims 1, 2, 4, 5, 8, 10, 11, 13-18, 21-26, 31, 38-47 were withdrawn from consideration and claim 34 was considered in the 16 May Office Action. Claims 16-18 were canceled and claims 1, 34 and 35 were amended in the 12 August Paper. Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 34, 35 and 38-47 are pending and claim 34 is under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 102

Rejection of claim 34 under 35 U.S.C. 102(b) as being anticipated by McEwan *et al.* (1996) *BioEssays* 19: 153-160 as evidenced by Bledsoe (2002) *Cell* 110: 93-105 is **withdrawn** in view of the amendment of the claim such that the system is now limited to comprising a first or second polypeptide comprising a Cys2-His2 zinc finger protein.

Claim Rejections - 35 USC § 112

Rejection of claim 34 under 35 U.S.C. 112, first paragraph, as containing new matter is **rendered moot** in view of the amendment of the claim such that it no longer requires that the ligand binds to both polypeptides.

In the remarks, Applicant contends that the limitation is supported by the specification as filed and cites teachings therefrom to support this contention. This argument is persuasive particularly in view of the teaching in the first full paragraph in page 2, which states, "[l]igand

mediated association and dissociation of proteins is also known, in which the ability of a protein to interact with another protein is dependent on the binding of one or both proteins" (emphasis added).

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 34 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claim has been amended such that the process steps are no longer recited in the claim. Although the process limitations do not distinguish the claimed invention from switching systems produced by other methods of providing a system having the same structural and functional properties as the switching system produced by the instant method, the limitations do evidence the hand of man. The amended claims, as written, do not sufficiently distinguish over switching systems that exist naturally (*e.g.*, estrogen receptor/Sp1/estrogen; see the discussion under "Claim Rejections - 35 USC § 102" herein below) because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor. See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by any one of Porter *et al.* (1997) *Mol. Endocrinol.* 11:1569-1580 as evidenced by Pratt *et al.* (1997) *Endocrine Rev.* 18:306-360 (the discussion of Porter *et al.* will refer to the HTML version of the article mailed herewith), Kobayashi *et al.* (1996) *J. Biol. Chem.* 271:12310-12316 or Perkins *et al.* (1993) *EMBO J.* 12:3551-3558 as evidenced by the Prosite Database entry PDOC00028, "Zinc finger C2H2-type domain signature and profile", available at us.expasy.org/cgi-bin/prosite-search-ac?PDOC00028.

Porter *et al.* teaches, "cooperative interactions of Sp1 and ER proteins play a role in regulation of at least five estrogen inducible genes, including c-*myc*, *CKB*, cathepsin D, RARα, and Hsp27" (page 3 of 12, lines 9-11). In Figure 2, Porter *et al.* demonstrates estrogen-induced expression from a reporter gene construct comprising an Sp1 binding site in cells cotransfected with an estrogen receptor and in Figure 8 Porter *et al.* demonstrates specific protein-protein interaction of the estrogen receptor with Sp1. In sum, Porter *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, an estrogen receptor) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, estrogen). Although Porter *et al.* teaches that the interaction of the estrogen receptor with Sp1 *in vitro* does not require estrogen (final sentence on page 8 of 12). Pratt *et al.*

teaches that the estrogen receptor is regulated by being held inactive in a complex including hsp90 and that binding of estrogen promotes dissociation of estrogen receptor from the complex and a conversion of the receptor to the DNA binding state (see especially the second full paragraph in the right column on page 343 as well as the paragraph bridging pages 307-308 through the paragraph bridging the left and right columns on page 308). In view of this and the showing of estrogen induced reporter gene expression in the intact cell discussed above, the skilled artisan would view the interaction of the estrogen receptor and Sp1 in the cell as "modulatable by a ligand". Of course, the estrogen receptor is a DNA binding protein (see, *e.g.*, Pratt *et al.*, page 308, paragraph bridging the left and right columns) and Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (see Prosite entry PDOC00028, the fourth bullet on page 2 of 4). Thus, the switching system of Porter *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Porter *et al.* as evidenced by Pratt *et al.* and Prosite Database entry PDOC00028.

Kobayashi *et al.* teaches cotransfection of SL2 cells with a reporter construct comprising a *CYP1A1* promoter and expression constructs encoding transcription factors AhR, Arnt and Sp1, and demonstrates a dramatic increase in reporter gene expression in response to the addition of the inducer molecule 3-MC (see especially the first paragraph in the left column on page 12312 and Figure 1B lanes 7 and 8). In addition, Kobayashi *et al.* demonstrates that the induction is much less in the absence of Sp1 or Ahr/Arnt (Figure 1B, lanes 3-6). Furthermore, Kobayashi *et al.* demonstrate the physical interaction of Sp1 protein with AhR and Arnt in immunoprecipitation experiments (see especially the first full paragraph in the right column on

page 12313 and Figure 4 and the caption thereto) and provide DNaseI footprinting data which suggest the interaction of AhR-Arnt and Sp1 bound to DNA (see especially the paragraph bridging pages 12314-12315 and Figure 8 and the caption thereto). In sum, Kobayashi *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, Ahr/Arnt) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, 3-MC). Furthermore, Kobayashi *et al.* teaches that the heterodimeric Ahr/Arnt complex is regulated in a manner similar to steroid hormone receptors, wherein Ahr exists in the cytoplasm bound to hsp90 and is translocated to the nucleus upon binding to inducer (see especially page 12310, left column, lines 8-18). Therefore, the interaction of the Ahr/Arnt with Sp1in the cell is modulatable by a ligand. In addition, Kobayashi *et al.* teaches that the Ahr/Arnt complex is DNA binding (*i.e.*, binds to the xenobiotic responsive element; see especially page 12310, left column, lines 8-19) and Prosite entry PDOC00028 teaches that Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (*Id.*). Thus, the switching system of Kobayashi *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Kobayashi *et al.* as evidenced by Prosite Database entry PDOC00028.

Perkins *et al.* teaches transfection of Jurkat cells with a reporter construct comprising a minimal NFκB/Sp1 enhancer and demonstrate that the Sp1 binding site is required for induction of the promoter by TNFα and PMA (inducers of NFκB; see especially the paragraph bridging the left and right columns on page 3554, Figure 3 and the caption thereto). In addition, Perkins *et al.* provides DNaseI footprinting and cross-linking data, which suggest direct protein-protein interaction of NF-κB and Sp1 (see especially the first full paragraph on page 3554, Figure 2 and

the caption thereto). This interaction is further evidenced by *in vivo* experiments which demonstrate that the TNFα and PMA induced expression require the close juxtaposition of the κB and Sp1 elements (see especially Figure 1B) and require that the elements be in a specific orientation with respect to one another (see especially Figure 4A and the discussion in the left column on page 3554, lines 18-36). In sum, Perkins *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, NF-κB) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, TNFα or PMA). Furthermore, Perkins *et al.* teaches that NF-κB is regulated in a manner similar to steroid hormone receptors, wherein NF-κB exists in a covert cytoplasmic form bound to an inhibitory protein IκB and treatment of cells with inducers such as TNFα and PMA results in release of NFκB into the nucleus and stimulation of NF-κB DNA binding (see especially the second full paragraph in the left column on page 3551). Therefore, the interaction of the NFκB with Sp1 in the cell is modulatable by a ligand. In addition, Perkins *et al.* teaches that NF-κB is DNA binding (*i.e.*, binds to the κB element; see especially the second full paragraph in the left column on page 3551 and the paragraph bridging pages 3551-3552) and Prosite entry PDOC00028 teaches that Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (*Id.*). Thus, the switching system of Perkins *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Perkins *et al.* as evidenced by Prosite Database entry PDOC00028.

As the art teaches switching systems comprising all of the elements of the switching system presently claimed, the claims are anticipated by the art and properly rejected under 35 USC §102(b).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER